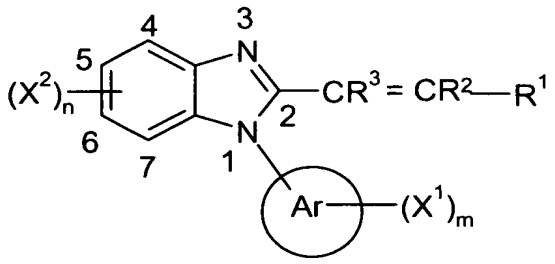
Claims

1. A compound of formula **I**:



(I)

or a pharmaceutically acceptable salt thereof, wherein

Ar is heteroaryl selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one to three N atom(s) in addition to said hetero atom, or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one to four N atom(s) in addition to said N atom; and

said heteroaryl being connected to the nitrogen atom on the benzimidazole through a carbon atom on the heteroaryl ring;

$\mathbf{X^1}$ is independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, [N-(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, [N, N-di(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, N-(C_1-C_4 alkanoyl)amino, N-(C_1-C_4 alkyl)-N-(C_1-C_4 alkanoyl)amino, N-[(C_1-C_4 alkyl)sulfonyl]amino, N-[(halo-substituted C_1-C_4 alkyl)sulfonyl]amino, C_1-C_4 alkanoyl, carboxy, (C_1-C_4 alkoxy)carbonyl, carbamoyl, [N-(C_1-C_4 alkyl)amino]carbonyl, [N, N-di(C_1-C_4 alkyl)amino]carbonyl, cyano, nitro, mercapto, (C_1-C_4 alkyl)thio, (C_1-C_4 alkyl)sulfinyl, (C_1-C_4 alkyl)sulfonyl, aminosulfonyl, [N-(C_1-C_4 alkyl)amino]sulfonyl and [N, N-di(C_1-C_4 alkyl)amino]sulfonyl;

$\mathbf{X^2}$ is independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4

alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, [N-(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, [N, N-di(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, N-(C_1-C_4 alkanoyl)amino, N-(C_1-C_4 alkyl)-N-(C_1-C_4 alkanoyl)amino, N-[(C_1-C_4 alkyl)sulfonyl]amino, N-[(halo-substituted C_1-C_4 alkyl)sulfonyl]amino, C_1-C_4 alkanoyl, carboxy, (C_1-C_4 alkoxy)carbonyl, carbamoyl, [N-(C_1-C_4 alkyl)amino]carbonyl, [N, N-di(C_1-C_4 alkyl)amino]carbonyl, N-carbamoylamino, cyano, nitro, mercapto, (C_1-C_4 alkyl)thio, (C_1-C_4 alkyl)sulfinyl, (C_1-C_4 alkyl)sulfonyl, aminosulfonyl, [N-(C_1-C_4 alkyl)amino]sulfonyl and [N, N-di(C_1-C_4 alkyl)amino]sulfonyl;

R^1 is selected from

hydrogen;

straight or branched C_1-C_4 alkyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, hydroxy, C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N, N-di(C_1-C_4 alkyl)amino;

C_3-C_8 cycloalkyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N, N-di(C_1-C_4 alkyl)amino;

C_4-C_8 cycloalkenyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N, N-di(C_1-C_4 alkyl)amino;

phenyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, [N-(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, [N, N-di(C_1-C_4 alkyl)amino]C_1-C_4 alkyl, N-(C_1-C_4 alkanoyl)amino, N-[(C_1-C_4 alkyl)(C_1-C_4 alkanoyl)]amino, N-[(C_1-C_4 alkyl)sulfonyl]amino, N-[(halo-substituted C_1-C_4 alkyl)sulfonyl]amino, C_1-C_4 alkanoyl, carboxy, (C_1-C_4 alkoxy)carbonyl, carbamoyl, [N-(C_1-C_4 alkyl)amino]carbonyl, [N, N-di(C_1-C_4 alkyl)amino]carbonyl, cyano, nitro, mercapto, (C_1-C_4 alkyl)thio, (C_1-C_4 alkyl)sulfinyl, (C_1-C_4 alkyl)sulfonyl, aminosulfonyl, [N-(C_1-C_4 alkyl)amino]sulfonyl and [N, N-di(C_1-C_4 alkyl)amino]sulfonyl; and

heteroaryl selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one to three N atom(s) in addition to said hetero atom; or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one to four N atom(s) in addition to said N atom; and

said heteroaryl being optionally substituted with one to three substituent(s) selected from $\mathbf{X^1}$;

$\mathbf{R^2}$ and $\mathbf{R^3}$ are independently selected from:

hydrogen;

halo;

C_1-C_4 alkyl;

phenyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N, N-di(C_1-C_4 alkyl)amino;

or $\mathbf{R^1}$ and $\mathbf{R^2}$ can form, together with the carbon atom to which they are attached, a C_3-C_7 cycloalkyl ring;

m is 0, 1, 2, 3, 4 or 5; and

n is 0, 1, 2, 3 or 4.

2. A compound according to claim 1, wherein

Ar is heteroaryl selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one or two N atom(s) in addition to said hetero atom, or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one to three N atom(s) in addition to said N atom; and

$\mathbf{X^1}$ is independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, N-(C_1-C_4 alkanoyl)amino, C_1-C_4 alkanoyl, carboxy, carbamoyl, [N-(C_1-C_4 alkyl)amino]carbonyl, [N,N-di(C_1-C_4 alkyl)amino]carbonyl, cyano, nitro, mercapto and (C_1-C_4 alkyl)thio;

X^2 is independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N,N-di(C_1-C_4 alkyl)amino, N-(C_1-C_4 alkanoyl)amino, [(C_1-C_4 alkyl)sulfonyl]amino, C_1-C_4 alkanoyl, carboxy, carbamoyl, N-carbamoylamino, cyano, nitro, mercapto and (C_1-C_4 alkyl)thio;

R^1 is selected from

hydrogen;

straight or branched C_1-C_4 alkyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, hydroxy, C_1-C_4 alkoxy and amino;

C_3-C_8 cycloalkyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy and amino;

C_4-C_8 cycloalkenyl optionally substituted with one to three substituent(s) wherein said substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N, N-di(C_1-C_4 alkyl)amino;

phenyl optionally substituted with one to three substituent(s) wherein the substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, (C_1-C_4 alkanoyl)amino, C_1-C_4 alkanoyl, carboxy, carbamoyl, (C_1-C_4 alkyl)thio, (C_1-C_4 alkyl)sulfinyl, (C_1-C_4 alkyl)sulfonyl, and aminosulfonyl; or

heteroaryl selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one or two N atom(s) in addition to said hetero atom; or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one to three N atom(s) in addition to said N atom; wherein

said heteroaryl being optionally substituted with one to three substituent(s) selected from X^1 of this claim;

R^2 and R^3 are independently selected from:

hydrogen;

halo;

C_1-C_4 alkyl;

phenyl optionally substituted with one to three substituent(s) wherein the substituents are independently selected from halo, C_1-C_4 alkyl, hydroxy, C1-C4 alkoxy, amino, N-(C_1-C_4 alkyl)amino and N,N-di(C_1-C_4 alkyl)amino;

or $\mathbf{R^1}$ and $\mathbf{R^2}$ can form, together with the carbon atom to which they are attached, a C_5-C_7 cycloalkyl ring;

m is 0, 1, 2, 3 or 4; and

n is 0, 1, 2 or 3.

3. A compound according to claim 2, wherein

Ar is selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one N atom in addition to said hetero atom, or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one or two N atom(s) in addition to said N atom; and

$\mathbf{X^1}$ is selected from halo, C_1-C_4 alkyl, halo-substituted C_1-C_4 alkyl, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkoxy, carbamoyl, [N-(C_1-C_4 alkyl)amino]carbonyl, [N,N di(C_1-C_4 alkyl)amino]carbonyl and cyano;

$\mathbf{X^2}$ is selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, hydroxy-substituted C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, N-formylamino, N-(C_1-C_4 alkanoyl)amino, [(C_1-C_4 alkyl)sulfonyl]amino, N-carbamoylamino, cyano and nitro; and

$\mathbf{R^1}$ is selected from

C_1-C_4 alkyl optionally substituted with one to three substituents wherein said substituents are independently selected from halo, hydroxy and amino;

C_5-C_7 cycloalkyl optionally substituted with one to three substituents wherein said substituents are independently selected from halo, hydroxy and amino;

phenyl optionally substituted with one or two substituent(s), said substituents being independently selected from halo, hydroxy, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, (C_1-C_4 alkyl)thio, C_1-C_4 alkylsulfonyl and amino; or

heteroaryl optionally substituted with one or two C_1-C_4 alkyl group(s), wherein said heteroaryl being selected from

a 5-membered monocyclic aromatic ring having one hetero atom selected from O, S and N and optionally containing one N atom in addition to said hetero atom, or

a 6-membered monocyclic aromatic ring having one N atom and optionally containing one or two N atom(s) in addition to said N atom;

R^2 and **R^3** are independently selected from

hydrogen;

halo;

C_1-C_4 alkyl; and

phenyl optionally substituted from halo, hydroxy, amino, C_1-C_4 alkyl and C_1-C_4 alkoxy;

or **R^1** and **R^2** can form, together with the carbon atom to which they are attached, a C_{5-6} cycloalkyl ring;

m is 0, 1, 2 or 3; and

n is 0, 1 or 2.

4. A compound according to claim 3, wherein

Ar is selected from pyridyl, pyrimidinyl, pyrazinyl thiazolyl, furyl, oxazolyl, isooxazolyl, thienyl, thiazolyl, isothiazolyl, pyrrolyl, imidazolyl, pyrazolyl and pyridazinyl;

X^1 is selected from halo, C_1-C_4 alkyl, halo-substituted C_1-C_4 alkyl, C_1-C_4 alkoxy, carbamoyl and cyano;

X^2 is selected from halo, C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, halo-substituted C_1-C_4 alkoxy, amino, N-(C_1-C_4 alkyl)amino, N, N-di(C_1-C_4 alkyl)amino, N-formylamino, N-(C_1-C_4 alkanoyl)amino, [(C_1-C_4 alkyl)sulfonyl]amino, N-carbamoylamino, cyano and nitro;

R^1 is selected from

(straight or branched) C_1-C_4 alkyl;

C_5-C_7 cycloalkyl;

phenyl optionally substituted with one or two substituent(s), said substituents being independently selected from halo, hydroxy, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo-substituted C_1-C_4 alkyl, (C_1-C_4 alkyl)thio and C_1-C_4 alkylsulfonyl; or

heteroaryl optionally substituted with one or two C_1-C_4 alkyl group(s), said heteroaryl being selected from pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, furyl, oxazolyl, isooxazolyl, thienyl, thiazolyl, isothiazolyl, pyrrolyl, imidazolyl and pyrazolyl;

$\mathbf{R^2}$ is selected from hydrogen, C_1-C_4 alkyl and phenyl;

$\mathbf{R^3}$ is selected from hydrogen, halo, C_1-C_4 alkyl and cyano;

or $\mathbf{R^1}$ and $\mathbf{R^2}$ can form, together with the carbon atom to which they are attached, cyclohexyl; and

m is 0, 1 or 2.

5. A compound according to claim 4, wherein

Ar is heteroaryl selected from pyridyl, pyrimidinyl, pyrazinyl and thiazolyl;

$\mathbf{X^1}$ is selected from fluoro, chloro, methyl, methoxy, trifluoromethyl, carbamoyl and cyano;

$\mathbf{X^2}$ is selected from fluoro, methyl, hydroxy, methoxy, ethoxy, isopropoxy, trifluoromethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-methylsulfonylamino, N-formylamino, N-acetylamino, N-carbamoylamino, cyano and nitro;

$\mathbf{R^1}$ is selected from methyl, isopropyl, cyclohexyl, phenyl, furyl, thienyl, pyridyl, imidazolyl and thiazolyl which are optionally substituted with one to three substituents selected from methyl, ethyl, isopropyl, methoxy, ethoxy, fluoro, chloro and hydroxy;

$\mathbf{R^2}$ is selected from hydrogen, methyl and phenyl;

or $\mathbf{R^1}$ and $\mathbf{R^2}$ can form, together with the carbon atom to which they are attached, cyclohexyl;

$\mathbf{R^3}$ is selected from hydrogen, fluoro and cyano; and

m is 0 or 1.

6. A compound according to claim 1, selected from

(*E*)-1-(2-Pyridyl)-2-styryl-1*H*-benzimidazole;

(*E*)-1-(4-Pyridyl)-2-styryl-1*H*-benzimidazole;

(*E*)-1-(2-Pyrimidyl)-2-styryl-1*H*-benzimidazole oxalate;

(*E*)-2-(2-Fluorostyryl)-1-(2-pyridyl)-1*H*-benzimidazole hydrochloride;

(*E*)-2-(2,6-Difluorostyryl)-1-(2-pyridyl)-1*H*-benzimidazole hydrochloride;

(*E*)-2-[2-(3-Furyl)ethenyl]-1-(2-pyridyl)-1*H*-benzimidazole;

(*E*)-1-(2-Pyridyl)-2-[2-(2-thienyl)ethenyl]-1*H*-benzimidazole;

(*E*)-5-Methyl-1-(2-pyridyl)-2-styryl-1*H*-benzimidazole;

(*E*)-5-Fluoro-1-(2-pyridyl)-2-styryl-1*H*-benzimidazole;

(*E*)-1-(2-Pyridyl)-2-styryl-5-methoxy-1*H*-benzimidazole oxalate;

(*E*)-2-[2-(Cyclohexyl)ethenyl]-5-methyl-1-(2-pyridyl)-1*H*-benzimidazole oxalate;

(E)-2-[2-(3-Furyl)ethenyl]-5-methyl-1-(2-pyridyl)-1*H*-benzimidazole oxalate;

(*E*)-5-Methyl-1-(2-pyridyl)-2-[2-(2-thienyl)ethenyl]-1*H*-benzimidazole oxalate;

(*E*)-2-[2-(Cyclohexyl)ethenyl]-5-fluoro-1-(2-pyridyl) -1*H*-benzimidazole;

(E)-2-[2-(3-Furyl)ethenyl]-1-(2-pyridyl)-5-methoxy-1*H*-benzimidazole oxalate;

(*E*)-5-Methoxy-2-[2-(2-methyl-3-furyl)ethenyl]-1-(2-pyridyl)-1*H*-benzimidazole.

7. A compound according to claim 1, selected from

(*E*)-2-[2-(Cyclohexyl)ethenyl]-1-(2-pyridyl)-1H-benzimidazole;

(*E*)-5-Fluoro-1-(2-pyridyl)-2-styryl-1*H*-benzimidazole;

(*E*)-1-(2-Pyridyl)-2-styryl-5-methoxy-1*H*-benzimidazole oxalate;

(*E*)-5-Methyl-1-(2-pyridyl)-2-[2-(2-thienyl)ethenyl]-1*H*-benzimidazole oxalate;

(*E*)-2-[2-(Cyclohexyl)ethenyl]-5-fluoro-1-(2-pyridyl) -1*H*-benzimidazole;

(*E*)-5-Methoxy-2-[2-(2-methyl-3-furyl)ethenyl]-1-(2-pyridyl)-1*H*-benzimidazole.

8. A pharmaceutical composition useful as anti-inflammatory and analgesic agents, which comprises a compound according to claim 1, and a pharmaceutically acceptable carrier.

9. A pharmaceutical composition for treating a disorder or condition in a mammal, selected from rheumatoid and osteoarthritis, pyrexia, asthma, bone resorption, cardiovascular diseases, nephrotoxicity, atherosclerosis, hypotension, shock, pain, cancer, Alzheimer disease, and other disorders and conditions, in which a pathological role of prostaglandins is implicated, comprising an amount of the compound of claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition, and a pharmaceutically acceptable carrier .

10. A method of treating a disorder or a medical condition in which prostaglandins are implicated as pathogens, in a mammalian subject, which comprises administering to a mammal an amount of compound of claim 1 or a pharmaceutically acceptable salt thereof, that is effective in treating said disorder or medical condition.

11. A method of treating a disorder or condition in a mammal, selected from rheumatoid and osteoarthritis, pyrexia, asthma, bone resorption, cardiovascular diseases, nephrotoxicity, atherosclerosis, hypotension, shock, pain, cancer, Alzheimer disease and other disorders and conditions, in which a pathological role of prostaglandins are implicated, comprising administering to a mammal in need of such treatment an amount of the compound of claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition, and a pharmaceutically acceptable carrier .